Year: 2019

The Challenge of Asymptomatic Bacteriuria and Symptomatic Urinary Tract Infections in Patients with Neurogenic Lower Urinary Tract Dysfunction

Tornic, Jure ; Wöllner, Jens ; Leitner, Lorenz ; Mehnert, Ulrich ; Bachmann, Lucas M ; Kessler, Thomas M

Abstract: PURPOSE We investigated prevalence of asymptomatic bacteriuria and incidence of symptomatic urinary tract infections (UTI) in patients with neurogenic lower urinary tract dysfunction (NLUTD) undergoing urodynamics and assessed predictors for symptomatic UTI. PATIENTS AND METHODS A prospective consecutive series of 317 patients (106 women, 211 men) with NLUTD was evaluated. Of them, 111 (35%) voided spontaneously, 141 (44%) relied on intermittent self-catheterization and 65 (21%) on an indwelling catheter. Before urodynamics, urine samples were collected by sterile catheterization for dipstick testing and urine culture. We assessed the association between patient characteristics and the occurrence of symptomatic UTIs following urodynamics in patients with asymptomatic bacteriuria and developed a prediction model based on the most important risk factors. RESULTS Urine cultures before urodynamics were negative in 123 (39%) and positive in 194 (61%) patients. (32%) and e (18%) were the most frequent bacteria. Of 194 patients with positive culture, 35 (18%) had at least one symptomatic UTI. In patients with a history of previous UTIs, the overall estimated probability of a symptomatic UTI was 45%, irrespective of the underlying neurological disorder. CONCLUSIONS About one out of five patients with asymptomatic bacteriuria will develop a symptomatic UTI in the follow-up year. This rather low overall probability precludes routine antibiotic prophylaxis or treatment in patients with NLUTD having asymptomatic bacteriuria as 4 out of 5 patients would be overtreated. However, in patients with a history of previous symptomatic UTIs antibiotic prescription might be justified.

DOI: https://doi.org/10.1097/JU.0000000000000555

Originally published at:
Tornic, Jure; Wöllner, Jens; Leitner, Lorenz; Mehnert, Ulrich; Bachmann, Lucas M; Kessler, Thomas M (2019). The Challenge of Asymptomatic Bacteriuria and Symptomatic Urinary Tract Infections in Patients with Neurogenic Lower Urinary Tract Dysfunction. Journal of Urology:101097JU0000000000000555.
DOI: https://doi.org/10.1097/JU.0000000000000555

Author's Accepted Manuscript

The challenge of asymptomatic bacteriuria and symptomatic urinary tract infections in patients with neurogenic lower urinary tract dysfunction

Tornic J, Wöllner J, Leitner L, Mehnert U, Bachmann LM, Kessler TM

DOI: 10.1097/JU.0000000000000555
Reference: JU-19-1414

To appear in: *The Journal of Urology*
Accepted Date: 11 September 2019

Please cite this article as: Tornic J, Wöllner J, Leitner L, Mehnert U, Bachmann LM, Kessler TM, The challenge of asymptomatic bacteriuria and symptomatic urinary tract infections in patients with neurogenic lower urinary tract dysfunction, *The Journal of Urology®* (2019), doi: 10.1097/JU.0000000000000555.

The Journal of Urology Publish Ahead of Print
DOI: 10.1097/JU.0000000000000555

The challenge of asymptomatic bacteriuria and symptomatic urinary tract infections in patients with neurogenic lower urinary tract dysfunction

Jure Tornic*[1], Jens Wöllner*[2], Lorenz Leitner[1], Ulrich Mehnert[1], Lucas M. Bachmann[3], Thomas M. Kessler[1]

* Shared first authorship

[1] Department of Neuro-Urology, Balgrist University Hospital, University of Zürich, Zürich, Switzerland

[2] Neuro-Urology, Swiss Paraplegic Center, Nottwil, Switzerland

[3] Medignition Inc., Research Consultants, Zürich, Switzerland

Email addresses:	jure.tornic@gmail.com,	ORCID 0000-0002-1831-4783
	jens.wöllner@paraplegie.ch,	ORCID 0000-0002-2518-8738
	lorenz.leitner@balgrist.ch,	ORCID 0000-0001-5764-3494
	ulrich.mehnert@balgrist.ch,	ORCID 0000-0001-7963-8477
	bachmann@medignition.ch	
	tkessler@gmx.ch,	ORCID 0000-0002-1991-5919

Corresponding author: Thomas M. Kessler, MD
Department of Neuro-Urology
Balgrist University Hospital
University of Zürich
Forchstrasse 340
8008 Zürich
Switzerland
Phone: +41 44 386 38 45
Fax: +41 44 386 39 09

Short title: Bacteriuria and urinary tract infections in neurogenic LUTD

Key words: bacteriuria, urinary tract infection, neurogenic lower urinary tract dysfunction, neuro-urology

Word count (Abstract): 244 Words, Word count (Total): 2472 Words

Abstract

Purpose: We investigated prevalence of asymptomatic bacteriuria and incidence of symptomatic urinary tract infections (UTI) in patients with neurogenic lower urinary tract dysfunction (NLUTD) undergoing urodynamics and assessed predictors for symptomatic UTI.

Patients and Methods: A prospective consecutive series of 317 patients (106 women, 211 men) with NLUTD was evaluated. Of them, 111 (35%) voided spontaneously, 141 (44%) relied on intermittent self-catheterization and 65 (21%) on an indwelling catheter. Before urodynamics, urine samples were collected by sterile catheterization for dipstick testing and urine culture. We assessed the association between patient characteristics and the occurrence of symptomatic UTIs following urodynamics in patients with asymptomatic bacteriuria and developed a prediction model based on the most important risk factors.

Results: Urine cultures before urodynamics were negative in 123 (39%) and positive in 194 (61%) patients. *Escherichia coli* (32%) and *Klebsiella pneumoniae* (18%) were the most frequent bacteria. Of 194 patients with positive culture, 35 (18%) had at least one symptomatic UTI. In patients with a history of previous UTIs, the overall estimated probability of a symptomatic UTI was 45%, irrespective of the underlying neurological disorder.

Conclusions: About one out of five patients with asymptomatic bacteriuria will develop a symptomatic UTI in the follow-up year. This rather low overall probability precludes routine antibiotic prophylaxis or treatment in patients with NLUTD having asymptomatic bacteriuria as 4 out of 5 patients would be overtreated. However, in patients with a history of previous symptomatic UTIs antibiotic prescription might be justified.

Introduction

Asymptomatic bacteriuria has a high prevalence in patients with neurogenic lower urinary tract dysfunction (NLUTD) and is considered to be a major risk factor for the development of symptomatic urinary tract infections (UTIs).[1-3] _ENREF_1 As a consequence, affected individuals have an increased risk for upper urinary tract damage and potentially life-threatening septicemia.[3] Furthermore, recurrent UTIs may negatively affect quality of life (QoL) due to aggravation of lower urinary tract symptoms (LUTS) and recurrent hospitalizations in the individual.[4]

As many patients with NLUTD need to rely on some form of catheterization (intermittent and indwelling) for bladder emptying, bacteriuria, leukocyturia, hematuria and positive nitrite are common and do usually not require an antibiotic therapy if no additional symptoms such as worsened LUTS, spasticity, fever, or pain are present. _ENREF_4[5] However, in daily clinical practice, patients without any symptoms are regularly treated with antibiotics based on "pathological" urine findings leading to increased risk of bacterial resistance and hence hampering appropriate antibiotic treatment in the case of a symptomatic UTI.[6] Thus, the management of asymptomatic bacteriuria and symptomatic UTIs remain a major challenge in neuro-urology raising the need to get a better insight into these issues.

We therefore aimed to investigate the prevalence of asymptomatic bacteriuria and incidence of symptomatic UTIs in patients with NLUTD undergoing urodynamic investigation (UDI) and assessed predictors for symptomatic UTIs.

Patients and Methods

Ethics statement: This study was approved by the local ethics committee of the University of Zürich (i.e. the Kantonale Ethikkommission Zürich, Switzerland) and it is registered with ClinicalTrials.gov (study registration number: NCT01297647). All participants gave written informed consent.

Patients: A consecutive series of 350 patients with NLUTD undergoing UDI were prospectively evaluated from June 2010 till December 2012. 33 patients were excluded due to incomplete datasets leaving 317 patients for analysis.

Measurements: Straight before UDI, urine samples were collected by sterile catheterization for dipstick testing (Combur® 10-Test, Roche Diagnostics International AG, Rotkreuz, Switzerland) and culture. At that time, no patient had clinical signs of symptomatic UTI. In addition, no patient received antibiotic treatment within 4 weeks before UDI. Patients were followed for 1 year and the rate of symptomatic UTI was calculated as the number of symptomatic UTI (defined as bacteriuria with concomitant symptoms / signs such as pain, dysuria, fever, new onset or worsening of incontinence, increasing spasticity, cloudy and/or malodorous urine and need for antibiotic treatment) during the year following the UDI.

Statistical analysis: The occurrence of symptomatic UTI per patient was counted. Student's t-test with a significance level of $p<0.05$ was used to compare mean differences between patients with asymptomatic bacteriuria prior to UDI who did and did not develop symptomatic UTI during follow-up. We bootstrapped a stepwise augmentation logistic regression model 10 times using the occurrence of at least one symptomatic UTI in the follow-up as the dependent and possible risk factors for the occurrence of symptomatic UTI as independent variables. Variables chosen in at least 80% of the final models were selected for the prediction model. Statistical analyses were performed using the Stata 14.2. statistical software package. (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.)

Results

Characteristics of the 317 patients are shown in Table 1. In the spinal cord injury (SCI) subgroup, the mean duration between SCI and the current evaluation was 17±11 years. 85 patients suffered from complete (American Spinal Injury Association (ASIA) Impairment Scale (AIS) A) and 102 from incomplete lesions (AIS B-D). Video-urodynamic findings are summarized in Table 2.

Dipstick urine testing before UDI revealed leukocytes in 48% (152/317) and/or nitrite positivity in 16% (52/317). Urine culture yielded any bacterial growth in 61% (194/317) and bacterial growth ≥10^5/mL in 42% (134/317) of the specimens. Sensitivity and specificity of dipstick urine testing regarding bacterial growth in urine culture are shown in Table 3.

In urine cultures incubated before UDI, more than 20 different bacterial strains were identified. *Escherichia coli* (32%; 62/194) and *Klebsiella pneumonia*e (18%; 35/194) were most frequently detected (Figure). Antibiotic susceptibility testing was performed in 154 out of 194 positive urine cultures and showed in 32% (49/154) resistance to trimethoprim-sulfamethoxazole (TMP-SMX), in 19% (29/154) resistance to nitrofurantoin, in 18% (28/154) resistance to ciprofloxacin, in 18% (27/154) resistance to cefuroxime, in 16% (24/154) resistance to amoxicillin/clavulanic acid, and in 1% (2/154) resistance to piperacillin/tazobactam.

Bacterial growth in urine cultures before UDI was found in 42% (47/111) of the patients voiding spontaneously, in 62% (88/141) of the patients performing aseptic intermittent self-catheterization (ISC), and in 91% (59/65) of patients with an indwelling catheter. Regarding the latter subgroup, the bladder was on intermittent and continuous drainage in 31% (20/65) and 69% (45/65) of patients, respectively. The distribution of the bacterial strains in the different groups was similar, i.e. *Escherichia coli* and *Klebsiella pneumoniae* were the most frequent germs. Remarkably, 82% (159/194) had no symptomatic UTI and 18% (35/194) suffered from at least one and 5% (10/194) had ≥3 symptomatic UTIs. Febrile UTIs occurred in 8% (15/194) and there was no association with the bladder emptying method.

To prevent recurrence of symptomatic UTIs, 29% (57/194) of the patients with asymptomatic bacteriuria proven before UDI were regularly taking L-methionine or cranberry. None of the patients included in this calculation was taking an antibiotic prophylaxis. Comparing these patients to those without prophylaxis, the mean rate of symptomatic UTIs per year was significantly ($p<0.001$) higher in the L-methionine and cranberry group, i.e. 0.8±0.2 per year versus 0.2±0.1 per year.

The history of previous UTIs (patients reporting at least one UTI prior to UDI) was the strongest parameter identified in the bootstrapping analysis. Table 4 shows the estimated probabilities along with actual percentages of symptomatic UTIs. Patients with a history of previous UTIs had an overall estimated probability of a symptomatic UTI of 45%. The probability distribution of the actual UTI frequencies during the 1-year follow-up of our patient cohort was comparable to the model.

Discussion

Main findings

In our prospective study including 317 patients with NLUTD, we found in more than 60% of the urine specimen an asymptomatic bacteriuria. Depending on the type of bladder emptying, the prevalence of asymptomatic bacteriuria was 42%, 62% and 91% in patients voiding spontaneously, performing aseptic ISC or having an indwelling catheter, respectively. However, the overall low incidence of symptomatic UTIs of less than 1 per year suggests that most of these patients are colonialized with bacteria and that only a very small proportion will develop UTIs even after an invasive investigation such as urodynamics. In our patient group, the sensitivity of dipstick testing was below 75% with a specificity of over 88%. This means that in our cohort approximately 1 out of 4 patients having pathological dipstick findings does not show any bacterial growth in the urine culture. Observing the UTI rates distinguished by bladder emptying method, patients on aseptic ISC had a twice to three times higher symptomatic UTI rate during follow-up than patients voiding spontaneously and patients with an indwelling catheter. The reason for this phenomenon is most likely multifactorial and might be explained by a beneficial effect of continuous bladder drainage on symptomatic UTI rate in patients with an indwelling catheter but also by suboptimal adherence to the ISC regime as some patients might have reduced ISC frequency to a 1-2 times per day basis on their own (ultimately leading to UTIs and other negative consequences). Remarkably, the history of previous UTI was a strong independent predictor indicating a higher risk for the development of symptomatic UTIs after UDI.

Findings in the context of existing evidence

In patients with NLUTD, the incidence of UTIs ranges from 1-10/year and the prevalence from 40-60%, depending on UTI definition, underlying neurological diseases and diagnostic criteria.[7] Darouiche et al.[8] investigated bacterial interference for prevention of UTIs in patients with NLUTD and reported a UTI incidence of 1.6/year which is slightly above our findings. However, relevant differences in patient population, UTI definition and assessments hinders further comparisons.

In contrast to the low rate of symptomatic UTIs, we identified a high number of bacterial growths in these asymptomatic patients. A similar high incidence of bacterial growth in samples from patients with NLUTD and relationship to bladder emptying method was described by Ronco et al.[9] _ENREF_13 and Ryu et al.[10] revealing a positive urine culture in 70% and 75%, respectively. In addition, the mode of bladder emptying was associated with the rate of positive urine cultures. Similar to our results, patients with a indwelling catheter (transurethral or suprapubic catheter) showed a bacterial growth of more than 80%.[10] Beside the impaired bladder function, the need for assistance for bladder emptying seems to be relevant for bacteriuria in these patients. Indeed, bladder emptying method was the primary determinant of UTIs in a prospective rehabilitation cohort study.[11]

An additional aim of our study was to evaluate the diagnostic criteria of UTIs in patients with NLUTD. Beside clinical signs, urinalysis and urine culture are currently recommended to diagnose UTIs in neurological patients.[2] _ENREF_13 However, dipstick testing has limited value,[2] despite of its wide use and might be more useful to exclude than to prove UTI in patients with NLUTD_ENREF_2 what is also underlined by the present study. Moreover, our findings are consistent with the results by Hoffman et al.[12] who observed in a sample of 56 SCI patients a sensitivity of 64% to predict significant bacteriuria. In addition, 30% of patients with positive leukocyte esterase and positive nitrite on dipstick testing had negative urine cultures.[12] Importantly, similar results were found in patients without an underlying neurological disease.[1, 2, 13] _ENREF_15

We found a wide distribution with more than 20 different uropathogens. Chabros et al.[14] analyzed more than 3200 urine samples of in-patients from a transplant and urological ward detecting more than 50 different microorganisms. In agreement with our results, *Escherichia coli*, *Klebsiella pneumoniae,* and *Proteus mirabilis* were the most frequently reported bacteria. Although our cohort consists of patients with NLUTD without immunosuppressive therapy, the bacteria distribution was similar.

Implications for practice

Despite a generally agreed definition of UTI in the neuro-urological patient is still lacking, there is consensus that signs and symptoms should be considered in addition to laboratory findings.[15] Ronco et al.[9] proposed a combination of clinical signs and leukocyturia to diagnose a UTI but could not determine satisfactory thresholds for bacterial and white blood cell count._ENREF_13 According to Massa et al.[16] clinical signs including cloudy and malodorous urine and leukocyturia seem to be the most accurate predictors for a symptomatic UTI.

To minimize the risk for antibiotic resistance, only symptomatic UTI should be treated in patients with NLUTD.[1, 2] The resistance rate for classic antibiotics (e.g. TMP-SMX, amoxicillin-clavulanic acid and ciprofloxacin) was 18-32% in our study. Bosch et al.[17] investigated the antibiotic resistance in outpatients suffering from symptomatic UTIs: In patients with complicated UTIs, the results revealed resistance rates of 68%, 65%, and 41% for TMP-SMX, amoxicillin and ciprofloxacin, respectively, nitrofurantoin showed a sensitivity rate of 73%. In the group with uncomplicated UTI, TMP-SMX and amoxicillin were resistant in 54% and 46%, whereas nitrofurantoin and ciprofloxacin had the highest sensitivity rate (89%).[17]

Prevention of recurrent symptomatic UTIs in the neuro-urological patient remains a challenge.[18]_ENREF_2 In our cohort, acidification and cranberry containing products were regularly taken by almost 30% of the patients which had significantly more symptomatic UTIs compared to the others reflecting the reason for prescribing these products.

In daily clinical practice, individualized concepts should be considered, avoiding screening for and treatment of bacteriuria in the absence of symptoms or signs of UTI, optimizing lower urinary tract function by proactive neuro-urological management and eliminating risk factors such as urinary stones, indwelling catheters and anatomical / mechanical obstruction. In the case that an antibiotic treatment is really needed, it should be conducted according to the results of the resistance testing. Additionally, statistical models, such as the one proposed by us might be used to select patients at higher risk assessment allowing the selection of individuals who might profit from antibiotic prescription.

Implications for research

Multi-drug-resistant uro-pathogenic microorganisms are significantly contributing to morbidity and mortality in patients with NLUTD causing a massive economic burden for every health care system.[19] To reduce the prevalence of these strains, unnecessary antibiotic therapies must be avoided, also considering prophylactic measures and alternative treatments involving "non-antibiotic" agents. As a physical action, bladder irrigations using indwelling or intermittent catheterization might be offered as described by Birkhäuser et al.[20] in a randomized controlled trial reporting that daily bladder irrigation applying tap water reduces the rate of antibiotic treatment in patients with ileal pouches._ENREF_21 Next generation DNA sequencing may improve diagnostic accuracy and enable direct targeting of bacterial biofilms to prevent recurrent UTIs by identifying bacteria which are not detectable using current techniques and by distinguishing bacterial strains with the capability of creating a biofilm from such which are not.[21] Bacteriophages are an accepted therapy for UTIs in several Eastern European countries and may become a valuable treatment option also in patients with NLUTD.[22-24] Moreover, several other treatment approaches such as probiotics,[25] homeopathy[26] and UroVaxom® (OM Pharma SA, Meyrin, Switzerland)[27] are promising and warrant further investigations. Finally, treatments such as electrical stimulation of the tibial, pudendal and sacral nerves making indwelling and intermittent catheterization redundant should be considered and closed-loop ontogenetic neuromodulation systems targeting specific neurons to control urinary tract function might completely revolutionize the field. [28]

Limitations of the study

Our study has several limitations. First, our department is a highly specialized university neuro-urology center. Thus, negative selection bias including more severe cases cannot be excluded and under-representation of non-SCI patients might be an issue. Second, there are no age and gender matched control groups which would allow for assessing different bladder management measures such as aseptic ISC, cranberry intake, low-dose antibiotics, etc. Third, subgroups were small for regression analysis so that they had to be merged (i.e. patients with complete SCI, incomplete SCI and neurological disorders other than SCI) to have a meaningful conclusion, so that no further differentiation on etiologies can be made. Last, the follow-up in this study is limited to 1 year. Considering that upper urinary tract damage generally evolves slowly over many years, longer follow-up would be needed to see if optimal management of recurrent UTIs has also a beneficial effect on long-term renal function.

Conclusions

Despite of the high incidence of bacterial growth in our patient group, the yearly incidence of symptomatic UTIs during follow-up was low as only one in five patients with asymptomatic bacteriuria developed at least one symptomatic UTI. These findings confirm that antibiotic treatment of UTIs in patients with NLUTD should only be initiated in presence of clinical signs and bacteriuria.

Additionally, asymptomatic bacteriuria, proven before invasive examinations of the lower urinary tract, does not justify a general recommendation for antibiotic prophylaxis or treatment. However, history of previous UTIs might be used in neurological patients with asymptomatic bacteriuria for symptomatic UTI risk assessment allowing the selection of individuals who might benefit from antibiotics.

Conflict of interest

None of the authors has a conflict of interest with this study.

Legends:

Table 1:

Patients characteristics.

Table 2:

Video-urodynamic parameters.

Table 3:

Sensitivity and specificity of dipstick urine testing in regard to bacterial growth in urine culture.

Table 4:

Probability distribution from a prediction model with the actual frequencies of symptomatic UTIs in patients with NLUTD and asymptomatic bacteriuria during the 1-year follow-up.

Figure:

Illustration of the distribution of the different bacterial strains detected in urine cultures before urodynamic investigation. *Escherichia coli* and *Klebsiella pneumoniae* were the most frequent bacteria. “Others” (35%, 68/194) include all bacterial germs (*Aerococcus sp., Citrobacter sp., Corynebacterium sp., Enterobacter sp., Enterococcus sp., Klebsiella sp., Lactobacillus sp., Morganella sp., Providencia sp., Pseudomonas sp., Serratia sp., Staphylococcus sp.*) which were proven in less than 2% (4/194) of positive urine specimen.

References

1. Panicker, J. N., Fowler, C. J., Kessler, T. M.: Lower urinary tract dysfunction in the neurological patient: clinical assessment and management. The Lancet Neurology, **14:** 720, 2015
2. Groen, J., Pannek, J., Castro Diaz, D. et al.: Summary of European Association of Urology (EAU) Guidelines on Neuro-Urology. Eur Urol, **69:** 324, 2016
3. Pannek, J., Wollner, J.: Management of urinary tract infections in patients with neurogenic bladder: challenges and solutions. Res Rep Urol, **9:** 121, 2017
4. Leitner, L., Sammer, U., Walter, M. et al.: Antibiotic prophylaxis may not be necessary in patients with asymptomatic bacteriuria undergoing intradetrusor onabotulinumtoxinA injections for neurogenic detrusor overactivity. Sci Rep, **6:** 33197, 2016
5. Bonkat, G., Pickard, R., Bartoletti, R., Cai T., Bruyère F., Geerlings S.E., Köves B., Wagenlehner F.: European Association of Urology (EAU) Guidelines on Urological Infections. Print. ISBN 978-94-92671-01-1. EAU Guidelines Office, Arnhem, The Netherlands. 2018
6. Koves, B., Cai, T., Veeratterapillay, R. et al.: Benefits and Harms of Treatment of Asymptomatic Bacteriuria: A Systematic Review and Meta-analysis by the European Association of Urology Urological Infection Guidelines Panel. Eur Urol, **72:** 865, 2017

7. Manack, A., Motsko, S. P., Haag-Molkenteller, C. et al.: Epidemiology and healthcare utilization of neurogenic bladder patients in a US claims database. Neurourology and urodynamics, **30:** 395, 2011
8. Darouiche, R. O., Green, B. G., Donovan, W. H. et al.: Multicenter randomized controlled trial of bacterial interference for prevention of urinary tract infection in patients with neurogenic bladder. Urology, **78:** 341, 2011
9. Ronco, E., Denys, P., Bernede-Bauduin, C. et al.: Diagnostic criteria of urinary tract infection in male patients with spinal cord injury. Neurorehabilitation and neural repair, **25:** 351, 2011
10. Ryu, K. H., Kim, Y. B., Yang, S. O. et al.: Results of urine culture and antimicrobial sensitivity tests according to the voiding method over 10 years in patients with spinal cord injury. Korean journal of urology, **52:** 345, 2011
11. Anderson, C. E., Chamberlain, J. D., Jordan, X. et al.: Bladder emptying method is the primary determinant of urinary tract infections in patients with spinal cord injury: results from a prospective rehabilitation cohort study. BJU Int, 2018
12. Hoffman, J. M., Wadhwani, R., Kelly, E. et al.: Nitrite and leukocyte dipstick testing for urinary tract infection in individuals with spinal cord injury. The journal of spinal cord medicine, **27:** 128, 2004
13. Buchsbaum, G. M., Albushies, D. T., Guzick, D. S.: Utility of urine reagent strip in screening women with incontinence for urinary tract infection. Int Urogynecol J Pelvic Floor Dysfunct, **15:** 391, 2004
14. Chabros, L., Mlynarczyk, G., Sawicka-Grzelak, A. et al.: Comparison of bacteria isolated from urinary tract infections in patients on transplant versus urologic wards. Transplantation proceedings, **43:** 3125, 2011

15. Averbeck, M. A., Rantell, A., Ford, A. et al.: Current controversies in urinary tract infections: ICI-RS 2017. Neurourol Urodyn, **37:** S86, 2018

16. Massa, L. M., Hoffman, J. M., Cardenas, D. D.: Validity, accuracy, and predictive value of urinary tract infection signs and symptoms in individuals with spinal cord injury on intermittent catheterization. The journal of spinal cord medicine, **32:** 568, 2009

17. Bosch, F. J., van Vuuren, C., Joubert, G.: Antimicrobial resistance patterns in outpatient urinary tract infections--the constant need to revise prescribing habits. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde, **101:** 328, 2011

18. Sihra, N., Goodman, A., Zakri, R. et al.: Nonantibiotic prevention and management of recurrent urinary tract infection. Nat Rev Urol, **15:** 750, 2018

19. Foxman, B.: Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med, **113 Suppl 1A:** 5S, 2002

20. Birkhauser, F. D., Zehnder, P., Roth, B. et al.: Irrigation of continent catheterizable ileal pouches: tap water can replace sterile solutions because it is safe, easy, and economical. Eur Urol, **59:** 518, 2011

21. Mouraviev, V., McDonald, M.: An implementation of next generation sequencing for prevention and diagnosis of urinary tract infection in urology. Can J Urol, **25:** 9349, 2018

22. Leitner, L., Sybesma, W., Chanishvili, N. et al.: Bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate: a randomized, placebo-controlled, double-blind clinical trial. BMC Urol, **17:** 90, 2017

23. Ujmajuridze, A., Chanishvili, N., Goderdzishvili, M. et al.: Adapted Bacteriophages for Treating Urinary Tract Infections. Front Microbiol, **9:** 1832, 2018

24. Sybesma, W., Zbinden, R., Chanishvili, N. et al.: Bacteriophages as Potential Treatment for Urinary Tract Infections. Front Microbiol, **7:** 465, 2016

25. Toh, S. L., Boswell-Ruys, C. L., Lee, B. S. B. et al.: Probiotics for preventing urinary tract infection in people with neuropathic bladder. Cochrane Database Syst Rev, **9:** CD010723, 2017

26. Pannek, J., Pannek-Rademacher, S., Jus, M. S. et al.: Usefulness of classical homeopathy for the prophylaxis of recurrent urinary tract infections in individuals with chronic neurogenic lower urinary tract dysfunction. J Spinal Cord Med**:** 1, 2018

27. Krebs, J., Fleischli, S., Stoyanov, J. et al.: Effects of oral immunomodulation therapy on urinary tract infections in individuals with chronic spinal cord injury-A retrospective cohort study. Neurourol Urodyn, 2018

28. Kessler, T. M., Birder, L. A., Gomery, P.: Neuromodulation of Urinary Tract Function. N Engl J Med, **380:** 2067, 2019

Table 1

Patients characteristics

Number of patients		317		(100%)
Sex				
Male		211		(67%)
Female		106		(33%)
Mean age [years](±SD)		56 ± 16		
Etiology of NLUTD				
Spinal cord injury		187		(59%)
	Cervical		58	
	Thoracic		104	
	Lumbar		25	
Multiple sclerosis		35		(11%)
Parkinson's disease		5		(2%)
Spina bifida		7		(2%)
Vertebral disc hernia		20		(6%)
Cauda equina syndrome		20		(6%)
Other		43		(14%)
Mean duration of disease [years]		18 ± 12		
Bladder emptying method				
Spontaneous voiding		111		(35%)
Aseptic ISC		141		(44%)
Indwelling catheter		65		(21%)
	Suprapubic		47	
	Transurethral		18	

ISC = Intermittent self-catheterization
SD = Standard deviation
NLUTD = Neurogenic lower urinary tract dysfunction

Table 2

Video-urodynamic parameters

Maximum cystometric capacity [mL] (±SD)	590 ± 260		
Compliance [mL/cmH$_2$O] (±SD)	71 ± 56		
Neurogenic detrusor overactivity (NDO)	186/317		(59%)
Detrusor sphincter dyssynergia	106/317		(33%)
Vesico-uretero-renal reflux	25		(8%)
Unilateral	21		(7%)
Grade I		6	
Grade II		9	
Grade III		5	
Grade IV		1	
Bilateral	4		(1%)
Grade I		2	
Grade II		2	
Grade III		0	
Grade IV		0	

SD = Standard deviation

Table 3

Sensitivity and specificity of dipstick urine testing in regard to bacterial growth in urine culture

	Sensitivity (95% CI)	**Specificity (95% CI)**
Leukocyturia	0.71 (0.64-0.77)	0.89 (0.82-0.94)
Nitrite positive	0.27 (0.21-0.34)	1.00 (0.97-1.00)
Combined leukocyturia and nitrite positive	0.32 (0.24-0.40)	1.00 (0.77-1.00)

CI = Confidence interval

Table 4

Probability distribution from a prediction model with the actual frequencies of symptomatic UTIs in patients with NLUTD and asymptomatic bacteriuria during the 1-year follow-up.

Predictors		Previous UTI		Overall
		no	yes	
Neurological disorder other than SCI	**n**	46	20	66
Estimated UTI probability		4%	56%	21%
Actual UTI frequency during follow-up		*2/14 (7%)*	*12/14 (86%)*	
Complete SCI	**n**	43	30	73
Estimated UTI probability		10%	47%	25%
Actual UTI frequency during follow-up		*4/18 (22%)*	*14/18 (77%)*	
Incomplete SCI	**n**	41	14	55
Estimated UTI probability		0%	21%	5%
Actual UTI frequency during follow-up		*0/3 (0%)*	*3/3 (100%)*	
Overall	**n**	130	64	194
Estimated UTI probability		5%	45%	18%
Actual UTI frequency during follow-up		*6/35 (17%)*	*29/35 (83%)*	

NLUTD = Neurogenic lower urinary tract dysfunction
SCI = Spinal cord injury
UTI = Urinary tract infection

Figure

Distribution of the different bacterial strains detected in urine cultures before urodynamic investigation